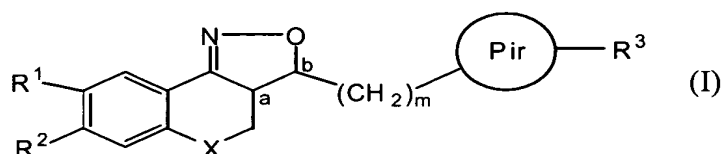


ABSTRACT
AMINO ISOXAZOLINE DERIVATIVES AND THEIR USE AS
ANTI-DEPRESSANTS

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The invention concerns substituted amino isoxazoline derivatives, more in particular tricyclic dihydrobenzopyranoisoxazoline, dihydroquinolinoisoxazoline, dihydronaphthalenoisoxazoline and dihydrobenzothiopyranoisoxazoline derivatives substituted on the phenylpart of the tricyclic moiety with primary, secondary and/or

10 tertiary amino groups, according to Formula (I)



wherein $X = CH_2$, $N-R^7$, S or O, R^1 , R^2 and R^3 are certain specific substituents, with the proviso that at least one of R^1 and R^2 is an amino radical of formula $N-R^{10}R^{11}$ wherein R^{10} and R^{11} are each a variety of radicals, Pir is an optionally substituted piperidyl or piperazyl radical and R^3 represents an optionally substituted aromatic homocyclic or heterocyclic ring system including a partially or completely hydrogenated hydrocarbon chain of maximum 6 atoms long with which the ring system is attached to the Pir radical and which may contain one or more heteroatoms selected from the group of O, N and S ; a process for their preparation, pharmaceutical compositions comprising them and their use as a medicine, in particular for the treatment of depression and/of anxiety and disorders of body weight. The compounds according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with additional α_2 -adrenoceptor antagonist activity and show a strong anti-depressant activity without being sedative. Compounds according to the invention are also suitable for treating depression, anxiety and body weight disorders. The invention also relates to novel combination of substituted amino isoxazoline derivatives according to the invention with antidepressants, anxiolytics and/or antipsychotics to improve efficacy and/or onset of action.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
9 October 2003 (09.10.2003)

PCT

(10) International Publication Number
WO 03/082878 A1

(51) International Patent Classification⁷: C07D 498/04,
498/14, 261/20, A61K 31/424, 31/5383, A61P 25/00 //
(C07D 498/04, 311:00, 261:00, (C07D 498/14, 311:00

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(21) International Application Number: PCT/EP03/03245

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(22) International Filing Date: 27 March 2003 (27.03.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
02076239.9 2 April 2002 (02.04.2002) EP

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(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

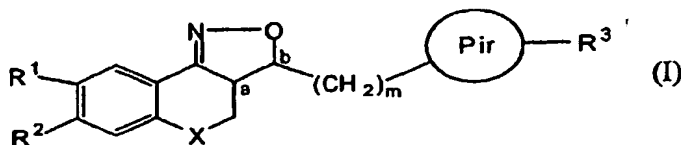
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Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: SUBSTITUTED AMINO ISOXAZOLINE DERIVATIVES AND THEIR USE AS ANTI-DEPRESSANTS.



(57) Abstract: The invention concerns substituted amino isoxazoline derivatives according to Formula (I) wherein X = CH₂, N-R⁷, S or O, R¹, R² and R³ are certain specific substituents, with the proviso that at least one of R¹ and R² is an amino radical of formula N-R¹⁰ R¹¹ wherein R¹⁰ and R¹¹ are each a variety of radicals, Pir is an optionally substituted, piperidyl or piperazyl radical and

R³ represents an optionally substituted aromatic homocyclic or heterocyclic ring system; pharmaceutical compositions comprising them and their use as a medicine, in particular for the treatment of depression and/of anxiety and disorders of body weight. The compounds according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with additional α₂-adrenoceptor antagonist activity